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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,412	07/11/2001	Shohei Koide	17027.003US1	8219

53137 7590 09/16/2009

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
09/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/903,412	KOIDE, SHOHEI	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7,8,55-57 and 59-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 7-8, 55-57 and 59-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Clams

Claims 1, 4, 7-8, 55-57 and 59-79 are pending and under examination in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102/§ 103

Claims 1, 4, 7-8, 55-57, 59-63, as amended and new claims 64-79 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lipovsek for reasons set forth by the Board's decision on 6/9/09 and reiterated below.

The Board in the decision made on 6/9/09 starting at page 10, states:

Lipovsek teaches an alignment of Fibronectin type III sequences in Figure 4, reproduced below with annotations which identify the locations of positions 7, 9 and 23 on the Fibronectin type III molecule: (Please see Figure 4 sequence alignment at page 10 of the decision. "FIG. 4 is a graph illustrating a sequence alignment between fibronectin type III protein domain and related protein domains" (Lipovsek, col. 6, 11. 31-33). 18. Lipovsek teaches a Canis familiaris (Cf)

sequence which is a Fibronectin type III molecule with a substitution of Asp 7 by neutral Asparagine, a substitution of Glu 9 by positively charged Arginine and a substitution of Asp 23 by Glutamine relative to the wild type human Fibronectin type III sequence (see Lipovsek, Figure 4, 8th line ("Cf") in alignment; FF 16). 19 Lipovsek teaches another sequence, RN, in which the Fibronectin type III molecule has a substitution of Asp 23 for Glutamic acid relative to the human fibronectin wild type sequence (see Lipovsek, Figure 4, 3rd line in alignment; FF 16). 20. Lipovsek teaches another sequence, HS CAP, in which the Fibronectin type III molecule has a substitution of Glu 9 by asparagine relative to the human fibronectin wild type sequence (see Lipovsek, Figure 4, 13th line in alignment; FF 16).

Principles of Law "[T]he PTO gives a disputed claim term its broadest reasonable interpretation during patent prosecution". In re Bigio, 381 F.3d 1320, 1324 (Fed. Cir. 2004). The court recognizes the fairness of reading claims broadly "before a patent is granted [since] the claims are readily amended as part of the examination process." Burlington Indus. v. Quigg, 822 F.2d 1581, 1583 (Fed. Cir. 1987). "Thus, a patent applicant has the opportunity and responsibility to remove any ambiguity in claim term meaning by amending the application". Bigio, 381 F.3d at 1324. Applying the broadest reasonable interpretation to

claims also "serves the public interest by reducing the possibility that claims, finally allowed, will be given broader scope than is justified." In re Am. Acad. of Sci. Tech. Ctr., 367 F.3d 1359, 1364 (Fed. Cir. 2004). "A rejection for anticipation under section 102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference." In re Paulsen, 30 F.3d 1475, 1478-79 (Fed. Cir. 1994); see Karsten Manufacturing Corp. v. Cleveland Golf Co., 242 F.3d 1376, 1383 (Fed. Cir. 2001) ("Invalidity on the ground of 'anticipation' requires lack of novelty of the invention as claimed ... that is, all of the elements and limitations of the claim must be shown in a single prior reference, arranged as in the claim."). "Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, on 'prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products". In re Best, 562 F.2d 1252, 1255 (CCPA 1977). "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his

claimed product." Id. Analysis Claim 1 requires a "modified" Fibronectin type III molecule. The Specification does not directly define "modified" (FF 11), but discloses that a "stabilizing mutation is defined herein as a modification or change in the amino acid sequence of the Fn3 molecule, such as a substitution of one amino acid for another" (Spec. 6, 11. 20-24; FF 12). Also, the Specification states that "[o]ne or more of the monobody loop region sequences of the Fn3 polypeptide vary by deletion, insertion or replacement of at least two amino acids from the corresponding loop region sequences in wild-type Fn3" (Spec. 7, 11.6-8; FF 15). Therefore, the word "modified" is reasonably interpreted in light of the Specification as representing a Fibronectin type III molecule in which there are one or more changes or substitutions in the amino acid sequence relative to the human wild type sequence. Claim 1 also requires that at least one of Asp 7, Asp 23, or Glu 9 be substituted with another amino acid, which the claim indicates functions as a "stabilizing mutation" (see claim 1; FF 13). Dependent claims 4 and 7 specifically identify replacement of Asp 7 or Asp 23 with asparagine as a mutation within the scope of claim 1 (see claims 4 and 7). Lipovsek teaches a human Fibronectin type III sequence which is identical to that disclosed in the Specification (FF 16-17). Lipovsek also teaches Fibronectin type III sequences

which are "modified" relative to the human sequence (FF 18-19). Specifically, Lipovsek teaches a Canis familiaris (Cf) sequence which is a Fibronectin type III molecule with a substitution of Asp 7 by Asparagine, a mutation of Glu 9 by Arginine and a substitution of Asp 23 by Glutamine relative to the wild type human FND (Fibronectin type III domain) sequence among other sequence differences (see Lipovsek, Figure 4, 8th line in alignment; FF 17- 18). Lipovsek also teaches another sequence, RN, in which the Fibronectin type III molecule has a substitution of Asp 23 by Glutamic acid relative to the human FND wild type sequence (see Lipovsek, figure 4, 3rd line in alignment; FF 17, 19). Lipovsek also teaches another sequence, HS CAP, in which the Fibronectin type III molecule has a substitution of Glu 9 by asparagine relative to the human FND wild type sequence (see Lipovsek, Figure 4, 13th line in alignment; FF 17, 20). The Cf, RN, and HS CAP sequences are reasonably interpreted as modified Fibronectin type III molecules with substitutions which would reasonably be believed as inherently stabilizing based upon the teachings of the Specification (FF 12-14). With regard to claims 4, 55, 57-59, 61, and 63, Lipovsek teaches the Cf Fibronectin type III sequence with a neutral asparagine at the position of Asp 7 (FF 18). With regard to claims 7, 8 and 57, Lipovsek teaches both

the Rn and Cf Fibronectin type III sequences with substitutions of one other amino acid residue at Asp 7, Asp 23, and Glu 9 (FF 18-19). With regard to claims 54 and 56, Lipovsek teaches a Cf Fibronectin type III sequence in which the Glu 9 is substituted with a positively charged arginine residue (FF 18). With regard to claims 55 and 58-60, Lipovsek teaches a Cf Fibronectin type III sequence in which the Asp 23 is substituted with a neutral glutamine residue (FF 18). With regard to claim 62, Lipovsek teaches a Hs CAP Fibronectin type III sequence in which the Glu 9 is substituted with asparagine (FF 20). In particular regarding the functional requirement that the mutation is a "stabilizing" mutation, we find that since the mutations disclosed by Lipovsek are identical to those required by the claims, the mutations would reasonably be expected to inherently function as "stabilizing" mutations in the absence of evidence to the contrary (FF 16-19). See In re Spada, 911 F.2d 705,708 (Fed. Cir. 1990) ("[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.") Conclusion of Law Claims 1, 4, 7, 8, and 54-63 are anticipated under 35 U.S.C. § 102(e) by Lipovsek.

Response to Arguments

Applicants state that Figure 4 of Lipovsek presents a sequence alignment between a fibronectin type III protein domain with sequences that are stated to be fibronectins from other sources, as well as sequences of related proteins. (See Figure 4, column 6, lines 31-33 and column 9, lines 9-12). The first row of Figure 4 depicts Hs FND (human fibronectin type III domain). Rows 2-9 depict alleged fibronectin sequences from other non-human sources (e.g., cow (row 2), rabbit (row 5), frog (row 7), dog (row 8) and horse (row 9). Rows 10-16 depicts sequences of other proteins (i. e., tenascin-C (row 10), tenascin precursor (row 11), collagen alpha precursor (row 13), collagen type 12 (row 14) and undulin 1 (row 16). The claims as amended are directed to modified human Fn3 molecules comprising a stabilizing mutation of at least one residue involved in an unfavorable electrostatic interaction as compared to the wild-type human Fn3 molecule. The stabilizing mutation is a substitution of at least one of amino acid residues 7, 23 or 9 with a neutral or positively charged amino acid residue. Applicant submits that the sequences presented in rows 10-16 of Figure 4 of Lipovsek are not Fn3 molecules. Further, the only human sequence presented in rows 1-9 is the human fibronectin type III domain sequence itself. The other sequences presented

in rows 2-9 are not human Fn3 sequences but instead are unmodified wild-type fibronectin sequences from other animals (e.g., cow, dog, horse, pig, rabbit or frog). Applicant submits that Lipovsek does not disclose each element of the claim under consideration, and a person or ordinary skill in the art would recognize differences between the claimed invention and the reference disclosure. Thus, because there are tangible differences between the invention as claimed and Lipovsek, Applicant submits that Lipovsek does not anticipate the currently pending claims.

In reply, as stated by the Board of Appeals above, Lipovsek teaches a human Fibronectin type III sequence which is identical to that disclosed in the Specification (FF 16-17). Lipovsek also teaches Fibronectin type III sequences which are "modified" relative to the human sequence (FF 18-19). Specifically, Lipovsek teaches a Canis familiaris (Cf) sequence which is a Fibronectin type III molecule with a substitution of Asp 7 by Asparagine, a mutation of Glu 9 by Arginine and a substitution of Asp 23 by Glutamine relative to the wild type human FND (Fibronectin type III domain) sequence among other sequence differences (see Lipovsek, Figure 4, 8th line in alignment; FF 17- 18). Lipovsek also teaches another sequence, RN, in which the Fibronectin type III molecule has a

substitution of Asp 23 by Glutamic acid relative to the human FND wild type sequence (see Lipovsek, figure 4, 3rd line in alignment; FF 17, 19). Lipovsek also teaches another sequence, HS CAP, in which the Fibronectin type III molecule has a substitution of Glu 9 by asparagine relative to the human FND wild type sequence (see Lipovsek, Figure 4, 13th line in alignment; FF 17, 20). The Cf, RN, and HS CAP sequences are reasonably interpreted as modified Fibronectin type III molecules with substitutions which would reasonably be believed as inherently stabilizing based upon the teachings of the Specification (FF 12-14).

With regard to claims 4, 55, 57-59, 61, and 63, Lipovsek teaches the Cf Fibronectin type III sequence with a neutral asparagine at the position of Asp 7 (FF 18). With regard to claims 7, 8 and 57, Lipovsek teaches both the Rn and Cf Fibronectin type III sequences with substitutions of one other amino acid residue at Asp 7, Asp 23, and Glu 9 (FF 18-19). With regard to claims 54 and 56, Lipovsek teaches a Cf Fibronectin type III sequence in which the Glu 9 is substituted with a positively charged arginine residue (FF 18). With regard to claims 55 and 58-60, Lipovsek teaches a Cf Fibronectin type III sequence in which the Asp 23 is substituted with a neutral glutamine residue (FF 18). With regard to claim 62, Lipovsek

teaches a Hs CAP Fibronectin type III sequence in which the Glu 9 is substituted with asparagine (FF 20). In particular regarding the functional requirement that the mutation is a "stabilizing" mutation, we find that since the mutations disclosed by Lipovsek are identical to those required by the claims, the mutations would reasonably be expected to inherently function as "stabilizing" mutations in the absence of evidence to the contrary (FF 16-19). See In re Spada, 911 F.2d 705,708 (Fed. Cir. 1990) ("[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.") Conclusion of Law Claims 1, 4, 7, 8, and 54-63 are anticipated under 35 U.S.C. § 102(e) by Lipovsek.

With regards to claims 64-79, Fig. 4, HsfND and the modifications recited by the Board above shows the different claim residues as disclosed by Lipovsek. For example, Fig. 4 shows HsFND which has valine (V) at position 1 (claims 64 and 78) and arg at position 6 (claims 65 and 79). The claims do not provide for the full sequence of the human Fn3 hence the native sequence is believed to be the same since the claim is modified only at positions 7, 23 and 9.

Claims 66 and 67 are disclosed by Lipovsek wherein position 7 is val or asn.

For claims 68-77, please see discussion above of the Board's decision.

It would be within the ordinary skill in the art given the homologs of a non-human Fn3 to substitute one amino acid in one or more positions from the homologous Fn3 e.g., cow, rabbit and other mammalian sequences to that of human Fn3 sequence. This is well-established in the art. Lipovsek also teaches substitutions at positions of the human Fn3 with random native residues.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated

from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639